

**WHAT IS CLAIMED IS:**

1. A method of alleviating the symptoms of, or prophylaxis of, an endothelin-related disease, which comprises:
  - a) extracting an aliquot of blood from the patient, subjecting the aliquot extracorporeally to at least two stressors selected from the group consisting of a temperature above or below body temperature, an electromagnetic emission and an oxidative environment; and
  - b) administering the aliquot of blood treated in step (a) to the patient, wherein the aliquot has a volume sufficient to alleviate said endothelin-related disorder.
2. The method of claim 1 wherein all of the stressors are simultaneously administered to the aliquot.
3. The method of claim 2, wherein the oxidative environment comprises applying an oxidizing agent to the aliquot.
4. The method of claim 3, wherein the oxidizing agent contains ozone gas, and the ozone gas is introduced into the blood aliquot in an amount which does not give rise to excessive levels of cell damage.
5. The method of claim 3, wherein the oxidizing agent comprises a mixture of ozone gas and medical grade oxygen, the ozone gas being contained in the mixture in a concentration of up to about 300 µg/ml.
6. The method of claim 5, wherein the ozone gas in the mixture is in a concentration of up to about 30 µg/ml.

8. The method of claim 5, wherein the mixture is applied to the aliquot at a flow rate of up to about 0.33 litres/min.
9. The method of claim 8, wherein the mixture is applied to the aliquot at a flow rate of from about 0.21 litres/min to about 0.27 litres/min.
10. The method of claim 2, wherein the electromagnetic emission comprises ultraviolet light having one or more UV-C band wavelengths.
11. The method of claim 2, wherein the temperature stressor is applied so that the temperature of at least part of the aliquot is in the range of from about -5°C to about 55°C.
12. The method of claim 2, wherein the mean temperature of the blood in the aliquot is in the range of from about 0°C to about 36.5°C.
13. The method of claim 2, wherein the temperature is in the range of from about 37°C to about 55°C.
14. The method of claim 13, wherein the temperature is  $42.5 \pm 1^\circ\text{C}$ .
15. The method of claim 2, wherein the volume of the aliquot is up to about 400 ml.
16. The method of claim 15, wherein the volume of the aliquot is about 10 ml.
17. The method of claim 2, wherein the aliquot is subjected to the stressors for a period of up to about 60 minutes.
18. The method of claim 17, wherein the aliquot is subjected to the stressors for a period of about 3 minutes.

19. The method of claim 2, wherein the blood is administered to the mammal by a method suitable for delivery selected from the group consisting of intra-arterial injection, intramuscular injection, intravenous injection, subcutaneous injection, intraperitoneal injection, and oral, nasal or rectal administration.
20. The method of claim 2, wherein the endothelin-related disorder is primary pulmonary hypertension.
21. The method of claim 2, wherein the endothelin-related disorder is glaucoma.
22. The method of claim 2, wherein the endothelin-related disorder is excessive angiogenesis.